Biomedicine Engineering and Public Health Studies
Volume 2, Issue 2, No. 1
Received 20 August 2023; Accepted 22 October 10, 2023
Published online 31 October 2023

Using decision trees to predict stroke risk factors

Luis Rafaeli Coutinho[1*], Josenilton da Silva Nascimento[2], Hidelbrando Ferreira Rodrigues[3]
[1]Postgraduate Program in Pharmacology, Federal University of Santa Catarina, Florianopolis, Brazil
[2]Florianopolis School of Public Health, Florianopolis, Brazil
[3]Tecnologia Institute of Exact Sciences and Technology, Federal University of Manaus, Itacoatiara, Brazil
E-mail: [1]*luisrafaelli29@gmail.com*, [2]*joseniltonfisio@gmail.com,* [3]*hrodrigues@ufam.edu.br*

Abstract. Stroke remains one of the main causes of disability and mortality in the world with complex socioeconomic consequences. Stroke is a heterogeneous disease with multiple causes, risk factors, contexts and additives to be researched. The residual effects of stroke have a negative impact on the quality of life by limiting physical, social and emotional health. Both for people with stroke and for their families and caregivers. Primary stroke prevention should expand actions to reduce risk factors that may be modifiable. This study provides an estimate by using the decision tree algorithm of stroke risk factors in the context of Primary Health Care in a survey carried out with the population of a Health Center located in the South region of Brazil. It aimed to identify predisposing factors to the risk of stroke, and to raise awareness about risk factors aimed at prevention. Lifestyle changes and a routine of healthy habits can reduce risk factors and the chances of a stroke. Public prevention policies should consider risk factors as a basis for discussing effective preventive measures and possible future directions in disease care. To improve primary prevention with specific strategies, depression and sleep quality require an in-depth investigation of their mechanisms in the development of stroke. Emerging technologies have the potential to collaborate with prevention.

Keywords. Disease prevention, primary health care, risk factors, stroke.

1. Introduction

Stroke is a complex medical and socioeconomic problem [1]. Stroke is a globally common disease that has detrimental effects on the individual and, more broadly, on society [2]. Stroke remains one of the main causes of disability and mortality in the world, especially in developing countries [3]. It remains the second leading cause of death and disability worldwide and more effective risk prevention approaches are needed to reduce the increased burden of stroke [4].

To improve stroke prevention, risk factors require in-depth investigation [5]. The main established risk factors for stroke are smoking, overweight/obesity, diet, dyslipidemia, diabetes mellitus, hypertension, kidney disease, coronary heart disease, congestive heart failure, valvular heart disease, atrial fibrillation and vascular disease. Multiple cardiovascular risk factors contribute to an increased risk of ischemic or hemorrhagic stroke [4].

The prevention of stroke and its associated risk factors has been one of the public health priorities worldwide [6]. Primary prevention should focus on reducing known modifiable risk factors. There is evidence that 80% or more of strokes are preventable. It is estimated that 45% of cases can be reduced by controlling blood pressure (BP). But there are a number of factors in stroke prevention that, if better recognized and controlled, can substantially reduce the risk of an episode [7].

Health systems are currently facing challenges in providing quality and high-value care to the population due to deficiencies in several dimensions in primary care [8]. Methods should be developed to systematically identify and treat related risk factors, collectively and individually, in all patients at risk of stroke [9]. From a public health perspective, preventive measures to reduce the risk of stroke may bring additional cross-cutting benefits [10]. Public awareness of stroke involving knowledge of risk factors is essential for the development of more specific primary prevention strategies [11].

However, there is a significant gap in knowledge about the effectiveness of various types of stroke prevention strategies in developing countries [10]. In this context, this work provides an estimation of risk factors for stroke (ischemic and hemorrhagic) using the Decision Tree algorithm, based on a Multivariate Logistic Regression (MLR) model. Its main objective is to identify predisposing factors to the risk of stroke and also as secondary objectives to raise awareness about predisposing factors and contribute to reflection on disease prevention.

2. Materials and Methods

The research was developed in Primary Health Care in the city of Florianópolis, Santa Catarina State, located in the south of Brazil. Florianópolis has an estimated population of 574,200 people and the highest Human Development Index (HDI-M) among Brazilian capitals (0.847). The municipal health network has 51 Health Centers (HC), distributed in 4 health districts. The CS Coqueiros, belongs to the Continente Health District, is divided into 03 coverage areas, with 03 family health teams and a population of 17679 users registered in the electronic health record used by the city.

Data collection took place at CS Coqueiros, between January 2017 and April 2018, with users aged between 35 and 74 years old who were in the waiting room of the basic health unit, in health promotion groups existing in the unit and in offices with a total sample of 132 patients. C.S Coqueiros users were invited to voluntarily answer a pre-elaborated instrument with questions related to stroke risk factors. A spreadsheet was created based on the questionnaire according to table 1 below.

Table 1. Collected stroke risk factors

Demographics	Age
	Gender
	Ethnicity
Cholesterol	High lipid profile
Arterial hypertension	Medical diagnostic
Arterial hypertension	Use of antihypertensive medication
Blood pressure checked at consultation	Systolic blood pressure (mmgHg)
Blood pressure checked at consultation	Diastolic blood pressure (mmgHg)
Smoking	Past
	Current
Family history	Cardiovascular diseases
	Arterial hypertension
Diabetes	Medical diagnosis
Atrial fibrillation	Medical diagnostic
BMI (body mass index)	Body mass index calculated between weight and height
Contraceptives	Use of contraceptive medications
Moderate physical activity practice	Reported practice
Alcoholism	Reported practice
Eating habits	Good diet reported
Migraine	Medical diagnostic
Depression	Medical diagnostic
Dementia / Cognitive Deficit	Medical diagnostic
Use of illicit drugs	Reported practice
Non-replenishing sleep	Reported sleep quality

The collected data were stored in the Microsoft Excel program and later analyzed. Statistical analysis was performed using the Action Stat Version 3.5.152.341 program. This cohort study was approved by the Research Ethics Committee of the Federal University of Santa Catarina (UFSC), based on Resolution 466/12, that determines the Guidelines and Regulatory Norms for Research involving Human Beings, according to opinion nº 2,537,066.

The proposed model is a development of work carried out by Coutinho and Rodrigues, 2020 [12]. Where RLM was performed to select the main factors of the sample collected using the Forward method. In the Forward method, the first selected variable is the one with the highest correlation with the response. The explanatory variable that presents the highest partial correlation coefficient will be included in the model if its contribution is statistically significant. The procedure continues for the other variables until either all variables are included in the model or a variable is rejected in the test of significance [13]. The risk factors selected by the RLM Forward method are shown in table 2.

Table 2. Stroke risk factors selected by MRL

Stroke risk factors	Description
Age	Age on assessment day
Gender	Gender: female, male
Ethnicity	Specific classification of collectives of individuals
Blood pressure	Systolic and diastolic blood pressure on the day of the consultation
Diabetes	Medical diagnostic
Body mass index (BMI)	Overweight and obesity assessed
Smoking	Smoking history
Stress	Self-reported stress
Contraceptive	Use of contraceptive medications

Thus, the stroke risk factors mentioned above were investigated by an analysis according to the Decision Tree technique using public domain software (R environment or simply R as usually called by its users) with open source code [14].

3. Results and Discussion

“Decision Trees” is one of the most popular data mining techniques. More commonly used to solve the task of data classification, the decision tree represents a model capable of guiding decision-making on determining the class to which an instance belongs and organizing a hierarchical model [15]. The training model took into account all the variables presented in the described data collection, while the test model, only the final variables selected by the RLM Forward method. According to the analysis of decision trees for the risk of stroke, the results are presented below according to figure 1, that brings a classification model in the form of a decision tree, for the risk of stroke according to the proposal.

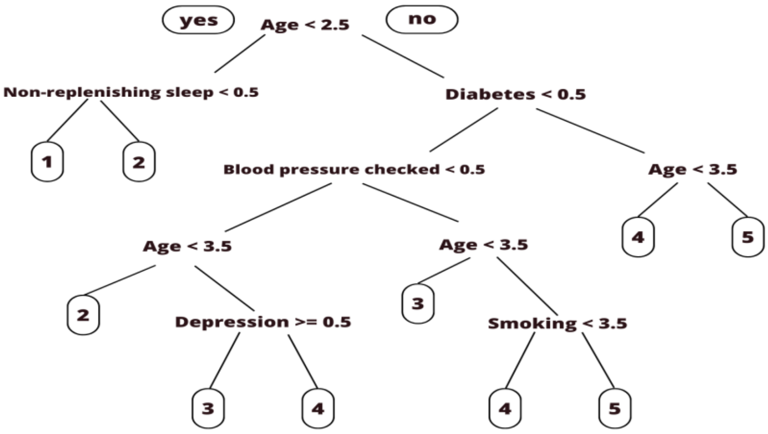

Figure 1. Performance of Decision Trees for Stroke Risk

The internal nodes of the tree refer to stroke risk classification attributes of the analyzed predisposing factors that were described. The construction of this model is carried out using an algorithm that interactively analyzes the descriptive attributes of a previously labeled data set, constituting a learning process for the classifier model. The decision tree is a model to be interpreted as IF THEN rules. Each of the rules derived from the trees is, in reality, a series of conditions verified on the internal nodes that make up the internal nodes of the tree (assumptions) that lead to decision making and represented in the leaf nodes of the tree (conclusions). Each path traversed deep in the decision tree generates an IF THEN rule; or alternatively, IF THEN ELSE rules can be designed for each subtree of the root node [15].

At this point, it is possible to see how the Decision Tree is applied as a classification model. Upon receipt of a test specimen, the decision tree must be traversed from the root to one of its leaves. At each internal node, the associated descriptive attribute must be verified in the test instance, and, depending on the value of such attribute, a node subtree will be chosen. Then, the process is repeated until the leaf node, with the label assigned to the test specimen, is reached [14]. According to the technique used, the stroke risk factors that were most relevant in the proposed model are listed and represented in table 3.

Table 3. Stroke risk factors selected by the decision tree technique

Stroke risk factors	Description
Age	Age on assessment day
Ethnicity	Specific classification of collectives of individuals
Blood pressure	Systolic and diastolic blood pressure on the day of the consultation
Diabetes	Medical diagnostic
Smoking	Smoking history
Depression	Medical diagnostic
Non-replenishing sleep	Reported sleep quality

Stroke prevention must include strategies for the entire population and for each individual, with priority on strategies for collective health. They must be directed to an integrated and unifying approach in order to optimize the efficiency of health systems in the preventive area [16]. Among the variables analyzed, the age factor, blood pressure measured at the time of consultation, diabetes, smoking, depression and non-restorative sleep in the proposed final model stood out. The elaboration of health policies with proposals for comprehensive primary prevention strategies should offer appropriate attention to predisposing factors to stroke and expand actions to reduce modifiable risk factors [17].

The Decision Tree analysis selected the factors depression and non-replenishing sleep and in the final classification model for stroke risk, which draw our attention. It did not include the risk factors of gender, ethnicity, BMI, stress and contraceptive use that were selected in the RLM method. Knowledge of stroke risk profiles can be useful to support different prevention strategies including identification and resolution of medical conditions. Particularly those with interactions that increase stroke risk thresholds [18]. Therefore, it is essential that healthcare professionals and policymakers understand the relevance of stroke risk factors to develop appropriate prevention strategies as well as rational allocation of healthcare resources according to the epidemiological profile of the population [19].

Stroke is a disease associated with aging and this non-modifiable risk factor increases the incidence of cerebrovascular events with age. The risk of having a stroke event doubles every decade after age 55 [3]. Elderly people may have a high burden of neurological disorders, in particular stroke and neurodegenerative diseases. In addition, the elderly are at greater risk of having comorbidities of two or more neurological diseases [16]. This represents a challenge with the aging of the population and the tendency towards a sedentary lifestyle [20].

Cellular aging is the most severe risk factor for neurodegenerative disease. Simultaneously, oxidative stress (OS) is a critical factor in the aging process, resulting from an imbalance between reactive oxygen and nitrogen species and the antioxidant defense system. Emerging evidence indicates that OS is a common cause of several age-related brain pathologies, including cerebrovascular diseases. Elevated OS disrupts endothelial functional ability by diminishing the bioavailability of nitric oxide (a vascular dilator), induces atherosclerosis, and impairs vasculature, which are all common characteristics of cerebrovascular disease [21]. As a major cause of morbidity and mortality globally, hypertension remains a serious threat to global public health. Regulation of the renin-angiotensin-aldosterone system (RAAS) controlling blood pressure, activation of the immune system triggering inflammation and production of reactive oxygen species, leading to oxidative stress and redox-sensitive signaling, have been implicated in the pathogenesis of hypertension. Thus, besides standard antihypertensive medications, which lower arterial pressure, antioxidant medications were tested to improve antihypertensive treatment. We review and discuss the role of oxidative stress in the pathophysiology of hypertension and the potential use of antioxidants in the management of hypertension and its associated organ damage [22].

Most strokes (60-70%) in all countries of the world are associated with high systolic blood pressure levels [23]. A genetic predisposition to higher BP has been associated with an increased risk of any ischemic stroke and its major subtypes [3]. Hypertension and its consequences are associated with more than 50% of ischemic and 70% of hemorrhagic strokes, but despite good blood pressure control, a 10% risk of recurrent cerebrovascular events remains. It is the most important risk factor for stroke; therefore, optimal blood pressure control is essential for stroke prevention. Hypertension is the most important risk factor for stroke; therefore, optimal blood pressure control is critical for stroke prevention [24]. Treating hypertension should be the priority target for both population-based and individual preventive interventions for primary prevention [16]. Lowering blood pressure by lifestyle modifications and antihypertensive medications reduces cardiovascular effects, morbidity, and mortality [25].

Diabetes is another major risk factor for stroke. Great advances have been made in the treatment of diabetes with new classes of medications, but it remains considered one of the main predisposing factors [7]. Diabetes causes several microvascular and macrovascular changes, often culminating in important clinical complications, one of them is stroke. Hyperglycemia confers a greater risk of stroke. People with diabetes have a 1.5 to 2 times greater risk of stroke compared to people without diabetes. Several mechanisms associated with diabetes lead to stroke, including large artery atherosclerosis, small vessel brain disease, and cardiac embolism [26]. And this increased risk is associated with negative clinical outcomes including increased mortality [27]. Furthermore, people with diabetes may have worse post-stroke outcomes and a higher risk of stroke recurrence than those without diabetes [26].

Selected as a risk factor for stroke in the proposed model, smoking occurs at all ages, both sexes and among different ethnic groups. Mechanisms linking smoking to vascular injury include endothelial damage, sympathetic activation, radical generation, and inflammation [28]. Smoking leads to the progression of atherosclerosis; increases hematocrit, platelet aggregation and raises blood pressure. They cause endothelial dysfunction and cause systemic inflammation. It covers products such as the new electronic cigarettes and hookah smoking [29]. Electronic cigarettes are tobacco derivatives and its use among adolescents is growing [30]. Smoking has a joint effect with other factors such as high blood pressure, diabetes, a sedentary lifestyle or the use of contraceptives, increasing the risk of cardiovascular problems [23]. All smokers should receive counseling and education about the importance of immediate smoking cessation. There are several methods and techniques available to help the smoking population quit or reduce tobacco consumption [31].

Depression was a stroke risk factor considered in our study. It plays an important role in increasing risk and may interact unfavorably with regard to cognition and prognosis compared with any other factor alone [32]. It is possible that the increased risk of stroke in depressed people is caused by underlying brain pathomechanisms specific to depressive disorder, such as brain inflammation, dysregulation of the hypothalamic-pituitary-adrenal axis, increased platelet reactivity, and autonomic dysfunction [33]. The underlying mechanisms linking depression to stroke are multifactorial. There is evidence that depression is linked to unhealthy lifestyles such as smoking and low physical activity which in themselves increase the risk of stroke. Furthermore, patients with depression may have reduced medication adherence for these conditions [34]. The side effects of certain antidepressants may also contribute to an increased risk of stroke [35]. Psychological health and major depressive disorder are increasingly recognized as impacting factors in cardiovascular disease. Depression management can serve as a cost-effective measure to mitigate the development of cardiovascular disease and the risk of stroke. More studies are needed to better understand these impacts and their mechanisms [36].

Some common factors that damage the brain over time are high blood pressure, smoking, and lack of sleep. Stress resulting from these factors accumulates and overloads the brain's compensatory repair mechanisms, resulting in dysfunction and disease [37]. Non-restorative sleep was a stroke risk factor selected in the proposed model. The risk of stroke should be considered in people with sleep problems and the mechanisms involving specific interferences [38]. The quality of sleep is influenced by several factors and is directly related to some diseases and emotional disorders [39]. Modern societies are experiencing a growing trend of reduced sleep duration, with nocturnal sleep below recommended health limits [40]. Sleep deprivation has been linked to an increased chance of having a stroke [41]. Inappropriate sleep duration is correlated with an increased odds of an ischemic stroke and an increased risk of stroke [42].

Insomnia is described as persistent problems with sleep initiation, maintenance, consolidation or quality despite sufficient sleep time and opportunity, leading to some kind of daily impairment [43]. There may be a genetic predisposition to short sleep duration and frequent symptoms of insomnia. In recent years, many studies have explored the relationship between sleep duration and stroke [42]. Furthermore, while some individuals adjust to challenges and change more effectively, others develop adjustment problems or struggle to manage their emotions, and this pressure can become stressful, increasing the risk of suffering a stroke [33]. The proportion of adults reporting insufficient sleep (<7 hours) in 2020 in the US was 32.8% [30].

The literature suggests that poor sleep, including insufficient sleep duration and disruption, is associated with poor short-term and long-term health outcomes [38]. In most healthy, normotensive people, BP decreases during sleep by 10 to 20% of mean awake values, a process known as a nocturnal BP drop. This phenomenon has emerged as a BP-related biomarker of healthy sleep physiology [44]. Unreduced nocturnal BP, defined as a difference between sleep and waking BP of <10%, has been associated with an increased risk for several cardiovascular diseases [45]. Sleep deprivation is found to affect the immune function, brain maturation, development of the body, metabolic process, and cognition, as well as maintaining normal homeostasis of the body [46]. Sleep is increasingly recognized as an integral component of cardiovascular health. The relationship between short and long sleep duration, as well as insomnia, with stroke risk is well-established. Recent work has highlighted how other sleep factors, such as sleep regularity (i.e., consistency of sleep timing), multidimensional sleep health, and circadian factors like chronotype and social jetlag, relate to stroke risk [47].

The circadian system is widely involved in the various pathological outcomes affected by time dimension changes. In the brain, the master circadian clock, also known as the “pacemaker,” is present in the hypothalamus's suprachiasmatic nucleus (SCN). The SCN consists of molecular circadian clocks that operate in each neuron and other brain cells. Many studies suggest that the circadian clock regulates blood pressure [48]. Circadian rhythms are endogenous oscillations with approximately a 24 hour period that allow organisms to anticipate the change between day and night. Disruptions that desynchronise or misalign circadian rhythms are associated with an increased risk of cardiometabolic disease [49]. Circadian disruption has become more prevalent in society due to the increase in shift work, sleep disruption, blue light exposure, and travel via different time zones [50]. Sleep-focused interventions (e.g., cognitive behavioral therapy for insomnia and sleep extension) may be effective to reduce stroke risk and disease burden [47].

There are numerous debates about the relationship between depression, anxiety, insomnia, perceived stress and stroke [33]. Differences in stroke epidemiology (including prevalence and order of importance of some of the modifiable risk factors) need to be considered in the search for gaps to establish a standardization of health care strategies and the achievement of internationally recommended goals [11]. We need to consider that there are disparities in disease patterns with variables in risk factors and socioeconomic disproportions in different territories that directly impact care and guarantee access to health services [10].

Preventive strategies for health risk factors addressing social determinants of health such as poverty, education, health insurance, social inclusion and non-discrimination, daily living conditions and access to quality health services are essential for effective primary stroke prevention [51]. Conduct monitoring to identify individuals in need of prophylactic drug therapy in conjunction with the population in need of lifestyle-related guidance and behavioral interventions across all population life cycles, regardless of the individual's disease risk [52]. Fostering a better chance to reduce deaths, disability and disparities in health care [53].

Preventive programs to reduce the incidence of stroke should include measures to reduce smoking, strategies to promote physical activity and healthy eating [18]. There is ample evidence demonstrating that improving the prevention and control of stroke risk factors with behavioral interventions to help people quit smoking, maintain a healthy diet and be physically active can reduces the possibility of developing a stroke [54]. Incorporating healthy daily activities into the routine has the potential to support lifestyle changes and requires persistence to promote benefits [2].

Care and educational interventions for the entire population are essential for stroke prevention [16]. A Mediterranean diet rich in olive oil, whole grains, fruits, vegetables and legumes and low in cholesterol, saturated fat and animal fat can reduce stroke by up to 40% or more in high-risk patients [55]. It is recommended to keep salt intake at 2 to 3 grams per day, limit meat intake (especially red meat) and avoid egg yolks. Reduce consumption of sugary drinks and alcohol [56]. Contributing to the reduction of the risk of cardiovascular diseases, including hypertension and diabetes [57].

In the age of big data and the internet of things, much health information is automatically electronically recorded and incorporated into databases [58]. The use of these records allows examining a large number of variables and can contribute to the development of stroke care strategies [59]. Emerging artificial intelligence and machine learning technologies are increasingly being used to predict the chances of a future stroke [6]. Algorithms based on analysis of risk factors may enable the development of predictive models that effectively surpass traditional clinical methods [5].

Primary stroke prevention can explore the applicability of different technologies [60]. Many neurological conditions share similar risk factors and preventive measures, which would mean increased attention and care [61]. Digital technologies, including smartphones and gadgets, which have become an integral part of our daily lives, have the potential to support clinical decision-making and improve risk factor prevention [62]. Precision medicine promises to transform healthcare for groups and individuals through early disease detection, refining diagnoses and personalized treatments [63].

4. Conclusions

Recognition of risk factors is important for stroke prevention. Among the variables analyzed in the study, the factors of age, blood pressure, diabetes, smoking, depression and non-replenishing sleep stood out. The classification model for the risk of stroke using the Decision Tree Algorithm selected the risk factors for non-replenishing sleep and depression who were not selected by the RLM method.

Depression has been characterized as an emerging public health problem and may interact unfavorably with regard to cognition and prognosis. sleep with the use of interactive technological resources at night. Lifestyle changes and the development of a healthy activity routine can contribute to the reduction of modifiable risk factors and the chances of a stroke.

Public prevention policies must consider all risk factors predisposing to stroke with due attention at the regional level and the population's adherence to the principles derived from them, expanding the discussion on the gaps in preventive models at the local level and possible future directions in related care to prevention. Greater understanding of the mechanisms that lead to sleep quality and the interaction of aspects related to major depression as stroke risk factors is needed. These risk factors have variables and require investigation to improve primary prevention. Emerging technologies such as big data, artificial intelligence, machine learning algorithms and the internet of things have the potential to collaborate in stroke care and help in the investigation of risk factors that require more evidence.

5. Limitations of the study

The present research provides important information about some stroke risk factors. However, this study has some limitations. Data collection took place in only one health center and the enrolled population present in this location. Differences in health indicators for the results of stroke risk factors identify some social determinants (low income, living in an area ofsocial vulnerability, social isolation, access and lack of guarantees in health care) that may help explain related disparities to risk factors in different territories. Which meant a limitation in our work. New studies exploring social determinants of health with the aforementioned risk factors and possible influences are recommended for a broader analysis of the cited topics.

Acknowledgements

Thanks to the staff, residents, students and patients of the C.S Coqueiros in the city of Florianópolis. All of you contributed in some way to the progress of this research.

Conflict of Interest Statement

We declare that there is no conflict of interest that could be perceived as detrimental to the impartiality of the research reported in this article. There is no external agency funding the project and there are no financial or personal relationships that could have influenced the interpretation of the results.

Authors' contributions

LRC coordinated the project from its inception, participated in data collection and contributed to the critical review of the written work. JNS contributed to providing study materials, handling data, checking and critically reviewing the written work. HFR contributed to the project design, development, statistical analysis, reproducibility of results and critical review of the written work. All authors contributed to the first version of the manuscript and all authors approved the final version.

References

[1] J. Addo et al., "Socioeconomic status and stroke," Stroke, vol. 43, no. 4, pp. 1186–1191, Apr. 2012. doi:10.1161/strokeaha.111.639732

[2] A.-H. Patomella et al., "Primary prevention of stroke: Randomised controlled pilot trial protocol on engaging everyday activities promoting health," BMJ Open, vol. 9, no. 11, Nov. 2019. doi:10.1136/bmjopen-2019-031984

[3] M. P. Driga et al., "The need for new biomarkers to assist with stroke prevention and prediction of post-stroke therapy based on plasma-derived extracellular vesicles," MDPI, https://www.mdpi.com/2227-9059/9/9/1226 (accessed Jun. 25, 2023). Biomedicines. 2021 Sep;9(9):1226. DOI: 10.3390/biomedicines9091226. PMID: 34572411; PMCID: PMC8466486.

[4] Y. Guo, "A new paradigm of 'real-time' stroke risk prediction and integrated care management in the Digital Health Era: Innovations Using Machine Learning and Artificial Intelligence Approaches," Thrombosis and Haemostasis, https://www.thieme-connect.com/products/ejournals/html/10.1055/a-1508-7980 (accessed Jun. 25, 2023).

[5] M. Wang et al., "Associations of genetic susceptibility and healthy lifestyle with incidence of coronary heart disease and stroke in individuals with hypertension," European Journal of Preventive Cardiology, vol. 29, no. 16, pp. 2101–2110, Jul. 2022. doi:10.1093/eurjpc/zwac135

[6] C. Ju et al., “Privacy-preserving technology to help millions of people: Federated prediction model for stroke prevention,” arXiv.org, https://arxiv.org/abs/2006.10517 (accessed Aug. 6, 2023).

[7] M. R. Azarpazhooh, C. Bogiatzi, and J. D. Spence, “Stroke prevention: Little-known and neglected aspects,” Cerebrovascular Diseases, vol. 50, no. 6, pp. 622–635, 2021. doi:10.1159/000515829

[8] L, Xi et al. Quality of primary health care in China: challenges and recommendations. The Lancet, v. 395, n. 10239, p. 1802-1812, 2020.

[9] O. Adeoye et al., “Correction to: Recommendations for the establishment of stroke systems of care: A 2019 update: A policy statement from the American Stroke Association,” Stroke, vol. 51, no. 4, pp. e187–e210, Apr. 2020. doi:10.1161/str.0000000000000225

[10] Y. V. Kalkonde, S. Alladi, S. Kaul, and V. Hachinski, “Stroke prevention strategies in the developing world,” Stroke, vol. 49, no. 12, pp. 3092–3097, Dec. 2018. doi:10.1161/strokeaha.118.017384

[11] S. C. Ouriques Martins et al., “Priorities to reduce the burden of stroke in Latin American countries,” The Lancet Neurology, vol. 18, no. 7, pp. 674–683, Jul. 2019. doi:10.1016/s1474-4422(19)30068-7

[12] L. R. Coutinho and H. F. Rodrigues, “Epidemiological analysis of the factors of risk of cerebrovascular accident by use of a risk estimator software in the primary attention,”, Physiotherapy in Health Care 3, https://www.semanticscholar.org/paper/AN%C3%81LISE-EPIDEMIOL%C3%93GICA-DOS-FATORES-DE-RISCO-DE-PELO-Coutinho-Rodrigues/b1d88d288dd287739041cab9be6cdf01d2ba88d0 (accessed Aug. 6, 2023

[13] Z. Bursac, C. H. Gauss, D. K. Williams, and D. W. Hosmer, “Purposeful selection of variables in logistic regression - source code for Biology and Medicine,” BioMed Central, https://scfbm.biomedcentral.com/articles/10.1186/1751-0473-3-17?report=reader (accessed Jun. 29, 2023).

[14] J. Chambers, “Software for Data Analysis,” Statistics and Computing, 2008. doi:10.1007/978-0-387-75936-4

[15] J. R. Quinlan, “Induction of decision trees - machine learning,” SpringerLink, https://link.springer.com/article/10.1007/BF00116251 (accessed Jun. 29, 2023).

[16] M. O. Owolabi et al., “Global synergistic actions to improve brain health for human development,” Nature News, https://www.nature.com/articles/s41582-023-00808-z (accessed Aug. 7, 2023).

[17] A. Scutelnic, M. R. Heldner, S. Jung, and M. Arnold, “The role of physical activity in primary stroke prevention,” Swiss Sports & Exercise Medicine, vol. 67, no. 4, Jan. 2020. doi:10.34045/ssem/2019/34

[18] R. Soto-Cámara et al., “Age-related risk factors at the first stroke event,” Journal of Clinical Medicine, vol. 9, no. 7, p. 2233, Jul. 2020. doi:10.3390/jcm9072233

[19] K. Kadier et al., “Association of sleep-related disorders with cardiovascular disease among adults in the United States: A cross-sectional study based on National Health and Nutrition Examination Survey 2005–2008,” Frontiers in Cardiovascular Medicine, vol. 9, Aug. 2022. doi:10.3389/fcvm.2022.954238

[20] B.-H. Chao et al., “Stroke prevention and control system in China: CSPPC-stroke program,” International Journal of Stroke, vol. 16, no. 3, pp. 265–272, Mar. 2020. doi:10.1177/1747493020913557

[21] V. Kumar, K. Bishayee, S. Park, U. Lee, and J. Kim, “Oxidative stress in cerebrovascular disease and associated diseases,” Frontiers in Endocrinology, vol. 14, Feb. 2023. doi:10.3389/fendo.2023.1124419

[22] M. Amponsah-Offeh, P. Diaba-Nuhoho, S. Speier, and H. Morawietz, “Oxidative stress, antioxidants and hypertension,” Antioxidants, vol. 12, no. 2, p. 281, Jan. 2023. doi:10.3390/antiox12020281

[23] V. L. Feigin et al., “Global, regional, and national burden of stroke and its risk factors, 1990-2019: A systematic analysis for the global burden of disease study 2019,” The Lancet. Neurology, https://pubmed.ncbi.nlm.nih.gov/34487721/ (accessed Aug. 7, 2023).

[24] A. J. S. Webb and D. J. Werring, “New insights into cerebrovascular pathophysiology and hypertension,” Stroke, vol. 53, no. 4, pp. 1054–1064, Apr. 2022. doi:10.1161/strokeaha.121.035850

[25] L. Lauder et al., “Hypertension management in patients with cardiovascular comorbidities,” European Heart Journal, vol. 44, no. 23, pp. 2066–2077, Nov. 2022. doi:10.1093/eurheartj/ehac395

[26] O. Mosenzon, A. Y. Cheng, A. A. Rabinstein, and S. Sacco, “Diabetes and stroke: What are the connections?,” Journal of Stroke, vol. 25, no. 1, pp. 26–38, Jan. 2023. doi:10.5853/jos.2022.02306

[27] R. Chen, B. Ovbiagele, and W. Feng, “Diabetes and stroke: Epidemiology, pathophysiology, pharmaceuticals and outcomes,” The American Journal of the Medical Sciences, vol. 351, no. 4, pp. 380–386, Apr. 2016. doi:10.1016/j.amjms.2016.01.011

[28] F. Z. Caprio and F. A. Sorond, “Cerebrovascular disease,” Medical Clinics of North America, vol. 103, no. 2, pp. 295–308, Mar. 2019. doi:10.1016/j.mcna.2018.10.001

[29] J. Klein, P. Diaba-Nuhoho, S. Giebe, C. Brunssen, and H. Morawietz, “Regulation of endothelial function by cigarette smoke and next-generation tobacco and nicotine products,” Pflügers Archiv - European Journal of Physiology, vol. 475, no. 7, pp. 835–844, Jun. 2023. doi:10.1007/s00424-023-02824-w

[30] C. W. Tsao and et al., “Correction to: Heart disease and stroke Statistics—2023 update: A report from the American Heart Association,” Circulation, vol. 147, no. 8, Feb. 2023. doi:10.1161/cir.0000000000001137

[31] N. E. Andrew et al., “The population effect of a national policy to incentivize chronic disease management in primary care in stroke: A population-based cohort study using an emulated target trial approach,” The Lancet Regional Health - Western Pacific, vol. 34, p. 100723, May 2023. doi:10.1016/j.lanwpc.2023.100723

[32] E. Douven et al., “Co-occurrence of depressive symptoms and executive dysfunction after stroke: associations with brain pathology and prognosis,” Journal of Neurology, Neurosurgery & Psychiatry, https://jnnp.bmj.com/content/89/8/859.info (accessed Aug. 7, 2023).

[33] E. Maalouf, S. Hallit, P. Salameh, and H. Hosseini, “Depression, anxiety, insomnia, stress, and the way of coping emotions as risk factors for ischemic stroke and their influence on stroke severity: A case–control study in Lebanon,” Frontiers, https://www.frontiersin.org/articles/10.3389/fpsyt.2023.1097873/full (accessed Jul. 4, 2023).

[34] M. Deng, S. Zhai, X. Ouyang, Z. Liu, and B. Ross, “Factors influencing medication adherence among patients with severe mental disorders from the perspective of mental health professionals,” BMC Psychiatry, vol. 22, no. 1, Jan. 2022. doi:10.1186/s12888-021-03681-6

[35] H. Koo et al., “Risk of cardiovascular events according to the tricyclic antidepressant dosage in patients with chronic pain: A retrospective cohort study,” European Journal of Clinical Pharmacology, vol. 79, no. 1, pp. 159–171, Nov. 2022. doi:10.1007/s00228-022-03421-z

[36] C. Krittanawong et al., “Association of Depression and Cardiovascular Disease,” The American Journal of Medicine, vol. 136, no. 9, pp. 881–895, Sep. 2023. doi:10.1016/j.amjmed.2023.04.036

[37] B. Sabayan et al., “The role of population-level preventive care for Brain Health in ageing,” The Lancet Healthy Longevity, vol. 4, no. 6, Jun. 2023. doi:10.1016/s2666-7568(23)00051-x

[38] K. Kadier et al., “Association of sleep-related disorders with cardiovascular disease among adults in the United States: A cross-sectional study based on National Health and Nutrition Examination Survey 2005–2008,” Frontiers in Cardiovascular Medicine, vol. 9, Aug. 2022. doi:10.3389/fcvm.2022.954238

[39] M. K. Fleming et al., “Improving sleep after stroke: A randomised controlled trial of digital cognitive behavioural therapy for insomnia,” Journal of Sleep Research, Jul. 2023. doi:10.1111/jsr.13971

[40] S. Garbarino, P. Lanteri, N. L. Bragazzi, N. Magnavita, and E. Scoditti, “Role of sleep deprivation in immune-related disease risk and outcomes,” Communications Biology, vol. 4, no. 1, Nov. 2021. doi:10.1038/s42003-021-02825-4

[41] L. Korostovtseva, “Ischemic stroke and sleep: The linking genetic factors,” Cardiology and Therapy, vol. 10, no. 2, pp. 349–375, Jun. 2021. doi:10.1007/s40119-021-00231-9

[42] H. Wang, J. Sun, M. Sun, N. Liu, and M. Wang, “Relationship of sleep duration with the risk of stroke incidence and stroke mortality: An updated systematic review and dose–response meta-analysis of prospective cohort studies,” Sleep Medicine, vol. 90, pp. 267–278, Feb. 2022. doi:10.1016/j.sleep.2021.11.001

[43] C. Sarmiento and C. Lau, “Diagnostic and statistical manual of mental disorders, 5th ed.: DSM-5,” *The Wiley Encyclopedia of Personality and Individual Differences*, pp. 125–129, Sep. 2020. doi:10.1002/9781119547174.ch198

[44] F. Routledge and J. McFetridge-Durdle, “Nondipping blood pressure patterns among individuals with essential hypertension: A review of the literature,” European Journal of Cardiovascular Nursing, vol. 6, no. 1, pp. 9–26, Mar. 2007. doi:10.1016/j.ejcnurse.2006.05.001

[45] M. Sieminski and M. Partinen, “‘non-dipping’ is equally frequent in narcoleptic patients and in patients with insomnia,” Sleep and Biological Rhythms, vol. 14, no. 1, pp. 31–36, Nov. 2015. doi:10.1007/s41105-015-0004-z

[46] B. Mete and L. Keskin, “Effects of sleep quality and insomnia severity on metabolic and anthropometric parameters in elderly individuals,” Cukurova Medical Journal, vol. 48, no. 3, pp. 806–814, Sep. 2023. doi:10.17826/cumj.1309925

[47] J. Belloir, N. Makarem, and A. Shechter, “Sleep and circadian disturbance in cardiovascular risk,” Current Cardiology Reports, vol. 24, no. 12, pp. 2097–2107, Nov. 2022. doi:10.1007/s11886-022-01816-z

[48] P. K. Kamat et al., “The Time Dimension to stroke: Circadian effects on stroke outcomes and Mechanisms,” Neurochemistry International, vol. 162, p. 105457, Jan. 2023. doi:10.1016/j.neuint.2022.105457

[49] L. J. Daniels, D. Kay, T. Marjot, L. Hodson, and D. W. Ray, “Circadian regulation of liver metabolism: Experimental approaches in human, rodent, and cellular models,” American Journal of Physiology-Cell Physiology, vol. 325, no. 5, Nov. 2023. doi:10.1152/ajpcell.00551.2022

[50] N. Schurhoff and M. Toborek, “Circadian rhythms in the blood–brain barrier: Impact on neurological disorders and stress responses,” Molecular Brain, vol. 16, no. 1, Jan. 2023. doi:10.1186/s13041-023-00997-0

[51] E. Reshetnyak et al., “Impact of multiple social determinants of health on incident stroke,” Stroke, vol. 51, no. 8, pp. 2445–2453, Aug. 2020. doi:10.1161/strokeaha.120.028530

[52] R. V. Krishnamurthi, V. L. Feigin, and T. Ikeda, “Global, regional, and country-specific lifetime risks of stroke, 1990 and 2016,” New England Journal of Medicine, vol. 379, no. 25, pp. 2429–2437, Mar. 2018. doi:10.1056/nejmoa1804492

[53] D. A. Levine, P. W. Duncan, M. N. Nguyen-Huynh, and O. G. Ogedegbe, “Interventions targeting racial/ethnic disparities in stroke prevention and treatment,” Stroke, vol. 51, no. 11, pp. 3425–3432, Nov. 2020. doi:10.1161/strokeaha.120.030427

[54] S. S. Virani et al., “Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association,” Circulation, vol. 141, no. 2, pp. e139–e596, Jan. 2020. doi:10.1161/cir.0000000000000746

[55] W. C. Willett and M. J. Stampfer, “Rebuilding the food pyramid,” Scientific American, vol. 288, no. 1, pp. 64–71, Jan. 2003. doi:10.1038/scientificamerican0103-64

[56] J. Spence, “Nutrition and risk of stroke,” Nutrients, vol. 11, no. 3, p. 647, Mar. 2019. doi:10.3390/nu11030647

[57] J. S. Chhabra et al., “The effect of nutrition on stroke risk: A systematic review,” Nutrition and Health, vol. 29, no. 2, pp. 255–267, Aug. 2022. doi:10.1177/02601060221122218

[58] M. Ryu, “Registry studies of stroke in Japan,” Journal of Atherosclerosis and Thrombosis, 2023. doi:10.5551/jat.rv22008

[59] R. C. Das et al., “Heart disease detection using ML,” 2023 IEEE 13th Annual Computing and Communication Workshop and Conference (CCWC), Mar. 2023. doi:10.1109/ccwc57344.2023.10099294

[60] Y. Yang, J. Zheng, Z. Du, Y. Li, and Y. Cai, “Accurate prediction of stroke for hypertensive patients based on medical big data and Machine Learning Algorithms: Retrospective study,” JMIR Medical Informatics, vol. 9, no. 11, Nov. 2021. doi:10.2196/30277

[61] Owolabi MO;Thrift AG;Mahal A;Ishida M;Martins S;Johnson WD;Pandian J;Abd-Allah F;Yaria J;Phan HT;Roth G;Gall SL;Beare R;Phan TG;Mikulik R;Akinyemi RO;Norrving B;Brainin M;Feigin VL; ;, “Primary stroke prevention worldwide: Translating evidence into action,” The Lancet. Public health, https://pubmed.ncbi.nlm.nih.gov/34756176/ (accessed Aug. 9, 2023).

[62] V. L. Feigin et al., “Digital Solutions for primary stroke and cardiovascular disease prevention: A mass individual and public health approach,” The Lancet Regional Health - Western Pacific, vol. 29, p. 100511, Dec. 2022. doi:10.1016/j.lanwpc.2022.100511

[63] E. Wong et al., “The Singapore National Precision Medicine Strategy,” Nature News, https://www.nature.com/articles/s41588-022-01274-x (accessed Aug. 7, 2023).